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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/550,173	04/14/2000	Norihisa Ooe	2185-0424-SP	8838

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EXAMINER
LAMBERTSON, DAVID A

ART UNIT	PAPER NUMBER
1636	17

DATE MAILED: 06/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/550,173	OOE ET AL.	
	Examiner	Art Unit	
	David A. Lambertson	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Peri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 11-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 11-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Receipt is acknowledged of a reply, filed April 3, 2003 as Paper No. 16, to the previous Office Action. Amendments were made to the claims. Specifically, claim 18 was cancelled.

Claims 1-9 and 11-17 are pending and under consideration in the instant application. Any rejection of record in the previous Office Action, Paper No. 15, mailed October 3, 2003, that is not addressed in this action has been withdrawn.

Because the Office Action maintains rejections that were cited in the previous Office Action and does not raise new grounds of rejection, this Office Action is made FINAL.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-9, 11 and 13-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bradfield *et al.* (US Patent No. 5,650,283; see entire document; henceforth Bradfield) in view of Waldman *et al.* (*Analytical Biochemistry* **258**: 216-222, 1998; see entire document; henceforth Waldman). **This rejection is maintained for reasons set forth in the previous Office Action, and in light of the response to applicant's arguments described below.**

Claims 2 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bradfield in view of Waldman, as applied to claims 1, 3-9, 11, and 13-17 above, and in further view of

Kushner *et al.* (US Patent No. 6,117,638; see entire document; henceforth Kushner). **This rejection is maintained for reasons set forth in the previous Office Action, and in light of the response to applicant's arguments described below.**

Response to Arguments Concerning Claim Rejections - 35 USC § 103

Applicant's arguments filed April 3, 2003 have been fully considered but they are not persuasive. Applicant's arguments concern the following points:

1. The Bradfield reference fails to teach securely maintaining the DNA that is transformed into the mammalian cell, rather teaching only transient transfection which is completely different from applicant's invention.

2. The Bradfield reference only generically teaches mammalian cells, and does not teach a specific mechanism for recovering mammalian cells that securely maintain DNA.

3. The Bradfield reference fails to teach the use of a full-length Ah receptor and a Dioxin Responsive Element in the mammalian system described therein.

4. That the teachings of Bradfield only apply to yeast systems, which is so different from the mammalian system described by Waldman that there can be no motivation to combine the references.

5. That neither the Bradfield nor the Waldman reference teaches two specific features of the instant invention, those being the "use of a minimum promoter which can function in an animal cell" and "both the reporter and the second selectable marker exist on the same molecule."

These arguments are applied to both rejections restated above.

The following point-by-point analysis of applicant's arguments sets forth the specific reasons as to why applicant's arguments are insufficient to overcome the rejection of the claims under 35 USC 103(a):

1. Applicant appears to be attacking the legitimacy of the Bradfield reference as if it reads as an anticipatory reference. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). It is clearly set forth in the previous Office Action that Bradfield does not teach securely maintaining DNA in the cell, which is why the Waldman reference is used as a secondary reference to show the obviousness of securely maintaining the DNA in the animal cell. Since applicant cannot attack the references as they stand individually, this argument is rendered moot.

2. The Bradfield clearly teaches a specific example of a mammalian cell (which by definition is an animal cell), and not just a generic teaching (see for example Ex. #6, column 35 to column 40). The method involves the construction of GAL4-AHR and GAL4-ARNT constructs (see for example column 37, line 1 to column 38, line 3) and the use of reporter constructs for the expression of β-galactosidase and CAT in response to activation of the receptor fusions in a ligand responsive manner (see for example column 39, lines 30-60, especially, lines 53-58). The specification further teaches a method of testing samples for the presence of activators (e.g., agonists- see for example column 2, lines61-64) of these receptors (see for example Ex. # 8, column 40-42); although the specification describes this assay based on the yeast system, the specification also indicates the system can be adapted for use with mammalian cells (see for

example column 42, lines 1-2), the adaptation being obvious from Ex. #6. The nature of the animal cell is a COS-1 cell (see for example column 38, line1), although other mammalian cells can be used (see for example 24, lines 7-9). The cell is then transformed with two separate vectors, one comprising the GAL4-receptor fusions, and one comprising a reporter operably linked to a TATA box core promoter and a separate selection marker (pG5BCAT; see for example column 38, lines 15-20). Finally, since these cells were specifically used in the assay as described, applicant must have recovered them for use. Thus, applicant's assertion that there is no specific teaching in the Bradfield reference concerning animal cells is unfounded.

3. Applicant's assertion that Bradfield does not teach either a full-length Ah receptor or a Dioxin Responsive Element is irrelevant, as the claims do not refer to either of these limitations. This is further irrelevant in light of applicant's definition of a ligand-responsive transcription control factor on page 13 starting at line 6, where it is indicated that said ligand-responsive transcription control factor can be a naturally-occurring gene or an artificially modified one, such as a protein to which a functional domain of a different transcription control factor (such as GAL4) is connected. Thus, the constructs described in Bradfield meet applicant's own definition of a ligand-responsive transcription control factor, thereby meeting the limitations of the claims. Finally, the ligand-responsive transcription factor recognition sequence taught by Bradfield meets the limitations of the claims as well because it responds to the GAL4 portion of said ligand-responsive transcription control factor.

4. Applicant attacks the motivation only in that the two teachings cannot be combined because they involve two very different systems. As indicated in part 2 above, applicant's assertion that Bradfield does not specifically teach animal cells is unfounded. As such, the only indicated

traversal for the combination of the elements is mooted by the fact that Bradfield does indeed specifically teach mammalian cells.

5. Bradfield teaches both elements that applicant alleges are not taught by either reference, as alluded to in part 2 above. Applicant defines a minimum promoter region as the core promoter, which contains the transcription initiation site and the TATA box (see for example page 17, line 7 of the instant specification). This is clearly what is used in the Bradfield reference (see for example column 38, lines 15-20), where the TATA box and core promoter are the only elements disclosed aside from the recognition sequence for the ligand-responsive transcription control factor, which must also be present as per the limitations of the claims. Furthermore, Bradfield teaches the use of two different plasmids in the assay, the GAL4-fusions and the reporter, pG5BCAT, which has a separate selectable marker (see for example column 38, lines 15-20). Finally, the Bradfield shows an example of a reporter expression plasmid and a reporter plasmid in Figure 11 (see for example column 3, lines 33-34 and figure 11), where the reporter has a second and separate selectable marker. Although, as applicants indicate, this *particular example* is for use in yeast, the ordinary skilled artisan, in light of the specific teachings in the specification concerning the use of mammalian cells, would understand that such a set of plasmids could be used in mammalian cells simply by exchanging the yeast selectable marker for a selectable marker that was functional in mammalian cells (e.g., tetracycline, zeocin, etc.) and which were known in the art at the time of the invention. Therefore, applicant's claim that these two elements are not taught by Bradfield is unfounded.

Because applicant's traversal of both rejections is based solely on the issues addressed above, both rejections under 35 USC 103(a) are maintained in view of the Examiner's response to applicant's arguments.

In conclusion, applicant has based their traversal of the rejection on elements that were purportedly not taught by the Bradfield reference, and equally not remedied by the combination of the Bradfield reference with the Waldman and Kushner references. However, as cited in the previous Office Action and clarified in the above response with regard to applicant's specific points of argument, Bradfield does indeed teach these elements. AS a result, the rejection is maintained as indicated in the previous Office Action.

Allowable Subject Matter

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (703) 308-8365. The examiner can normally be reached on 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David A. Lambertson
June 6, 2003

DAVID GUZO
PRIMARY EXAMINER